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ORIGINAL ARTICLE

Improvement of cytotoxicity of mitoxantrone and daunorubicin by candidone, tephrosin, and bavachinin

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Abstract

Background Flavonoids have been demonstrated to have the ability of sensitizing cancer cells to chemotherapy and inverse multidrug resistance via various mechanisms, such as modulating of pumps. The therapeutic effect of candidone, tephrosin, and bavachinin in treatment of cancer, particularly to overcome multidrug resistance (MDR) is largely unknown. The capacity of these agents in sensitization of MDR cells is investigated in the current work.

Methods and results We analyzed the impact of candidone, tephrosin, and bavachinin, as chemosensitizer on cell cytotoxicity, *P-gp* and *ABCG2* mRNA expression level on two multidrug resistant cells, ABCG2 overexpressing human epithelial breast cancer cell line (MCF7/MX), and P-gp overexpressing human gastric adenocarcinoma cell line (EPG85.257RDB). The inhibitory concentration of 50% (IC50) of daunorubicin in EPG85.257RDB cells in combination with IC10 of Bavachinin, Tephrosin, and Candidone were 6159 ± 948, 4186 ± 665, 730 ± 258 nM, and this data in MCF7/MX cell were 1773 ± 534, 7160 ± 405 and 3340 ± 622 nM respectively. These three flavonoids dose-dependently decreased the viability of MCF7/MX and EPG85.257RDB and significantly ($p < 0.05$) decreased IC50 of daunorubicin and mitoxantrone except Tephrosin in MCF7/MX cells. Candidone and Bavachinin were the most potent chemosensitizer in EPG85.257RDB and MCF7/MX cells respectively. Flavonoids did not reduce mRNA expression of P-gp and ABCG2 after 72 h treatment, except Candidone in EPG85.257RDB and Bavachinin in MCF7/MX cells.

Conclusions This effect is not time-dependent, and flavonoids have their own patterns that are cell-dependent. In general, tephrosin, candidone, and bavachinin had the potential of sensitizing MDR cells to mitoxantrone and daunorubicin.

Keywords MDR1 · ABCG2 · Flavonoid · Multidrug resistant · Real-time pcr

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